

REMARKS

I. AMENDMENTS TO THE SPECIFICATION

The specification at paragraphs [0059]-[0062] has been amended. Specifically, the terms "bacteria" and "bacterial strains" are replaced with "yeast" and "yeast strains," respectively. These amendments are made to correct translation errors in view of the as-filed specification as a whole; for example, paragraphs [0059]-[0061] disclose Embodiment 4 (Transformation of yeast) and paragraph [0062] discloses fermentation measurement in the yeast transformants of Embodiment 4. No new matter has been introduced.

II. STATUS OF CLAIM

Claims 1, 16, and 18 have been amended to clarify the claimed subject matter. The claim language is supported by the as-filed specification, e.g., paragraphs [0027] and [0040]. No new matter has been introduced.

Claims 1-7 and 16-18 are currently pending.

III. Rejection under 35 U.S.C. § 103(a)

Applicant respectfully request reconsideration and withdrawal of the 35 U.S.C. § 103(a) rejection of claims 1-7 and 16-18 over WO 99/14335 to Porro et al. for at least the following reasons.

The Office asserted that WO 99/14335 does not explicitly teach a single embodiment of the claimed transformed bacteria or yeast, but WO 99/14335 suggests a transformed yeast having a single integrated copy of a lactate dehydrogenase gene operably linked to a pyruvate decarboxylase promoter. Office Action, page 5. In addition, in response to the argument of unpredicted beneficial results from using the claimed transformant presented in the Reply to Final Office Action filed December 10,

2009, the Office asserted that “increased efficiency of lactic acid production” is not clearly described in the specification, and contends that “a skilled artisan would understand that integrating the expression cassette into the genome of the host organism provides advantages such as not losing the plasmid during culture.” Office Action, page 6. Applicant respectfully disagrees with the Office’s above allegations in at least the following aspects.

In the present specification, the inventors presented the unexpected results related to the claimed transformants. Specifically, in Embodiment 5, the inventors measured the L-lactic acid production from the claimed transformants. Tables 1 and 2 present these results of KCB-27, KCB-210, and KCB-211, the transformants of IF02260 containing the lactate dehydrogenase (LDH) gene integrated into the genome. See paragraphs [0062]-[0063].

The attached Declaration of Toru ONISHI under 37 C.F.R. § 1.132 (“Declaration”) evidences that the L-lactic acid production the claimed transformants disclosed in the present application showed an unexpectedly increased efficiency as compared to the prior art. Specifically, as shown in Table 1 of the Declaration, the claimed transformants, containing a single copy of an LDH gene incorporated into the chromosome, produced lactic acid in the amount larger than, or at least similar to, the amount of lactic acid produced from the yeast transformants carrying multiple copies of an LDH gene, as disclosed in Porro et al.¹ (“Ref. 1”); Adachi et al.² (“Ref. 2”); and WO

¹ Porro et al., *Development of metabolically engineered Saccharomyces cerevisiae cells for the production of lactic acid*, Biotechnol. Prog. Vol. 11, No. 3, pp. 294-298 (1995) (submitted in the IDS filed March 24, 2009).

² Adachi et al., *Modification of metabolic pathways of Saccharomyces cerevisiae by the expression of lactate dehydrogenase and deletion of pyruvate decarboxylase genes for the*

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99/14335. See Declaration at paragraphs 10-12 and Table 1. Contrary to the above-mentioned Office's position, the increased efficiency of the claimed transformants is not due to the loss of plasmids into the cell culture medium in the prior art, e.g., in WO 99/14335. See Declaration at paragraph 13. The claimed transformants therefore showed an increased efficiency of lactic acid production from introducing only a single copy of an LDH gene compared to the yeast cells introducing multiple copies of an LDH gene in Refs. 1, 2, and WO 99/14335.

One of ordinary skill in the art, relying on the prior art including WO 99/14335, at the time of invention, would recognize an increased efficiency of lactic acid production due to introducing multiple copies of an LDH genes to the cells. Refs. 1 and 2, and WO 99/14335, provide no reason to expect an increased efficiency of lactic acid production from the chromosomally-integrated LDH gene. For the sake of arguments, and not by admission, even if the benefits of the integrated transformants of the claimed invention were recognized by WO 99/14335, a skilled artisan certainly would have pursued them instead of focusing entirely on the plasmid transfections of yeast, as taught in WO 99/14335. One of ordinary skill in the art at the time of invention, therefore, would not have had expected successful results from incorporating a single copy of an LDH gene into the host chromosome such that it is under the control of a genomic pyruvate decarboxylase gene promoter on the host chromosome and a pyruvate decarboxylase gene on the host chromosome is replaced with the single copy of the LDH gene.

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lactic acid fermentation at low pH value, J. Ferment. Bioeng. Vol. 86, No. 3, pp. 284-289 (1998) (submitted in the IDS filed March 24, 2009).

With regard to claims 4 and 5, the Office merely asserted that WO 99/14335 teaches the gene coding for lactate dehydrogenase may be of any species. Office Action, page 8. WO 99/14335 neither discloses nor suggests the specific sequences recited in claims 4 and 5. Without a showing that these sequences are in the prior art, the Office should not reject these claims. Moreover, the unexpected results of the claimed transformants, as discussed above, also support the patentability of claims 4 and 5.

For at least the foregoing reasons, claims 1-7 and 16-18 are allowable over WO 99/14335.

IV. Conclusion

In view of the foregoing remarks, Applicant respectfully requests reconsideration of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

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Dated: March 23, 2010

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Attachments:

- 1) Declaration of Toru ONISHI under 37 C.F.R. § 1.132; and
- 2) Information Disclosure Statement under 37 C.F.R. § 1.97(b).